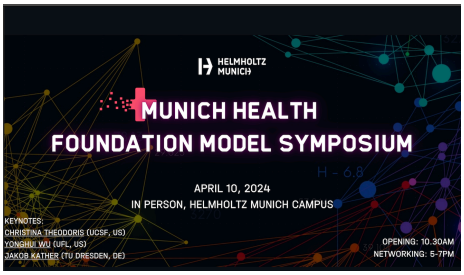

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Discovery of immunological cellular neighborhoods from protein markers in spatial tumor data

Introduction

Spatial imaging of single cells and their protein markers in multiple tumor tissues offers detailed insights into the mechanisms of tumor-microenvironment interactions. The identification and characterization of cellular neighborhoods are vital to elucidating these mechanisms. However, existing approaches for cellular neighborhood analyses resort to predefined cell types or coarse, neighborhood-wide cell marker aggregations, failing to preserve the marker information at the single-cell level resolution.

Method

We developed Cellohood - the first permutation-invariant, transformer-based autoencoder designed to model cellular neighborhoods explicitly. Cellohood compresses information about each cell and its marker expression for a given neighborhood, providing representations of the cellular neighborhoods. Based on these representations, we derived novel cellular neighborhood prototypes. Cell types, protein markers, and spatial arrangement patterns describe each identified prototype. Consequently, patients can be described by the abundance of cellular neighborhood prototypes and their mutual arrangements.

Results

We showcased the performance of Cellohood by applying it to multiple datasets obtained using different spatial imaging technologies, including:
- Mouse spleen lupus CODEX data from Goltsev et al.,
- Breast cancer IMC data from Jackson et al.,
- NSCLC and TNBC IMC Data from the Immucan consortium.

Patient representations obtained by Cellohood correlate with disease stages, types/histologies, and patient prognosis. Additionally, spatial analysis has shown that the neighborhood representation encodes different tissue architectures and tumor infiltration patterns.

Conclusions

Thanks to transformer-based generative modeling, Cellohood is the first model to utilize complete cell marker information during training without resorting to coarse, neighborhood-wide approximation. Results on the multiple datasets obtained using different technologies demonstrated that Cellohood enables marker-driven discovery of cellular-microenvironment interactions and their clinical implications.

Primary author: MOŻEJKO, Marcin (University of Warsaw)

Co-authors: GOGOLEWSKI, Krzysztof (Faculty of Mathematics, Informatics, and Mechanics, University of Warsaw); Dr SCHULZ, Daniel (Department of Quantitative Biomedicine, University of Zurich, Zurich, Switzerland, Institute for Molecular Health Sciences, ETH Zurich, Zurich, Switzerland); Dr ELING, Nils (Department of Quantitative Biomedicine, University of Zurich, Zurich, Switzerland, Institute for Molecular Health Sciences, ETH Zurich, Zurich, Switzerland); Ms KRAWCZYK, Joanna (Faculty of Mathematics, Informatics and Mechanics, University of Warsaw); Ms MOŻWIŁŁO, Aleksandra (Faculty of Mathematics, Informatics and Mechanics, University of

Warsaw); Ms DANIEL, Michelle (Department of Quantitative Biomedicine, University of Zurich, Zurich, Switzerland, Institute for Molecular Health Sciences, ETH Zurich, Zurich, Switzerland); Ms MALINOWSKA, Roksana (Faculty of Mathematics, Informatics and Mechanics, University of Warsaw); Ms FEDORCZYK, Izabela (Faculty of Mathematics, Informatics and Mechanics, University of Warsaw); Mr STAUB, Eike (Merck KGaA, Darmstadt, Germany); Dr MORFOUACE, Marie (Merck KGaA, Darmstadt, Germany); Dr HONG, Henoch (Merck KGaA, Darmstadt, Germany); Prof. BODENMILLER, Bernd (Department of Quantitative Biomedicine, University of Zurich, Zurich, Switzerland, Institute for Molecular Health Sciences, ETH Zurich, Zurich, Switzerland); SZCZUREK, Ewa (Helmholtz Munich)

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